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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/627,132 | 07/25/2003 | Kanwarpal S. Dhugga | 0864R3 | 3306 |

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| EXAMINER | |
|---|---|
| IBRAHIM, MEDINA AHMED | |
| **ART UNIT** | **PAPER NUMBER** |
| 1638 | |

DATE MAILED: 09/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/627,132 | DHUGGA ET AL. | |
| | Examiner | Art Unit | |
| | Medina A. Ibrahim | 1638 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *10 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *13-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

Applicant argues against the restriction requirement between Groups I-III in the Office action of 03/11/05. Applicant specifically argues that since the polynucleotide of Group I encodes the polypeptide of Group II, and the method of Group III uses the polynucleotide of Group I, the restriction requirement between inventions I, II, and III is improper. Applicant asserts that the inventions I-III are not independent as required by the MPEP 806.04 and 808.01 because they are connected by claims 9 and 11, drawn to a method of modulating the level of cellulose synthase by introduction and modified expression of a polynucleotide of claim 1. Applicant further asserts the search and consideration of all claims in this application would not be burdensome. Applicant, therefore, requests that inventions I-III be considered as a single invention and examined in this application.

These arguments have been considered but are not deemed persuasive because the three inventions define patentably distinct inventions and searching them together in a single application would be burdensome, as stated in the last Office action. Inventions I and II are related as product and process of making the product. MPEP § 806.05(f) states that the inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process. In the instant case, the isolated polypeptide of Group II can be prepared by another and materially different process than that of Group I, such as

chemical synthesis. MPEP 806 (B) also states, " (w)here inventions are related as disclosed but are distinct as claimed, restriction may be proper". In addition, there is search burden in both sequence databases and non-patent literatures. The polypeptide claims include polypeptides with 20 contiguous amino acids of the sequence identified. This search requires an extensive analysis of the art retrieved in a sequence search and will require an in-depth analysis of technical literature, as stated in the last Office. Searching, therefore is not coextensive. Therefore, the restriction requirement between Group I and II is proper and according to the MPEP.

Inventions I and III are related as product and process of using the product. MPEP § 806.05(h) states that the inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. In the instant case, the isolated polynucleotide of Group I can be used in a in a materially different process of using that product, such as in hybridization assay. MPEP 806 (B) also states, "(w)here inventions are related as disclosed but are distinct as claimed, restriction may be proper". In addition, the method of Group III requires the step of identifying from a population of maize plants mutagenized with the Mu transposable element, which is not required by the method of Group I. Therefore, it is clear that the search of the invention of Group I will not reveal all arts relevant to the invention of Group III, therefore each invention requires a separate search. Therefore, the restriction requirement between Group I and III is proper and according to the MPEP.

Furthermore, the instant specification does not disclose that the isolated polypeptide of Group II can be used in the method of Group III. The isolated polypeptide of Group II is not required by the method of Group III. Therefore, it is clear that the search of the invention of Group II will not reveal all arts relevant to the invention of Group III, therefore each invention requires a separate search. Therefore, the restriction requirement between Group I and III is proper.

In addition, contrary to Applicant's argument, inventions I-III are not connected by claims 9 and 12 because transformation of plant cells with the polynucleotide of claim 1 in a recombinant expression cassette and culturing/regenerating the plant cells are not required by any of the inventions II and II. Therefore, the restriction requirement between inventions I, II, and III is proper and according to MPEP.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-15 are pending. Claims 13-15 are withdrawn from consideration as being directed to the non-elected invention. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Applicant's response filed 06/10/05 in reply to the Office action of 03/11/05 has been entered. Claims 1-2 and 8-11 are amended. Claims 1-12 are examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All previous objections and rejections not set forth below have been withdrawn. The Double patenting rejection has been withdrawn in view of Applicant's amendment to

the claims to recite 90% sequence identity. The polynucleotide sequence of SEQ ID NO: 30 of the instant application and the polynucleotide sequence (SEQ ID NO: 30) of the copending application 10/209, 059 are not 90% identical.

***Claim Rejections - 35 USC § 112***

Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the isolated nucleic acid comprising the polynucleotide of SEQ ID NO: 29 encoding SEQ ID NO: 30, a recombinant expression cassette comprising said polynucleotide, transgenic plant and plant cell comprising said polynucleotide, and a method of transforming plant/cell with said polynucleotide, does not reasonably provide enablement for an isolated nucleic acid comprising a polynucleotide having at least 90% sequence identity with SEQ ID NO: 29, wherein the polynucleotide encodes a functional cellulose synthase, antisense sequences of all polynucleotides encoding SEQ ID NO: 30, and a complementary polynucleotide thereof, said polynucleotides having the ability to modulate cellulose synthase level in a transgenic plant. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. This rejection is repeated for the reasons of record as set forth in the last Office action of 03/11/05. Applicant's arguments filed 06/10/05 have been considered but are not deemed persuasive.

Applicant correctly states that a patent application need not disclose every claimed species, but that the disclosure must be sufficiently teach to those of ordinary skill in the art for how to make and use the invention, without undue experimentation.

Applicant, however, asserts that the instant specification provides detailed guidance for how to make and use the invention as broadly claimed. Applicant points to pages 24- 25 and 47-49 of the specification for guidance regarding sequence modifications. Applicant asserts that one of skill in the art would have no problem in making conservative sequence substitutions to obtain the claimed polynucleotides, given the disclosed conserved domains of cellulose synthase as shown in the multiple sequence alignment provided in Exhibit 1. Applicant, therefore, requests that the rejection be withdrawn (response, pp. 12-12).

These arguments are not persuasive because the specification is not enabling for the broad scope of the claims. While the specification provides general guidance regarding a single amino acid conservative substitution to produce variants, the scope of the instant claims is not so limited. The claims encompass polynucleotides with multiple nucleotide modifications any where along the full-length sequence (SEQ ID NO: 29), and a method of using said polynucleotides to alter cellulose synthase level in a transgenic plant. For example, in Applicant's working examples, four CesA genes (CesA1, CesA4, CesA5, and CesA8) were individually expressed under the same promoter in maize. The results show that plants from the transgenic events generated using the CesA8 gene were significantly taller in comparison to the control plants containing a GUS gene, while a reduction in height was observed with the CesA1, and other two genes, CesA4 and CesA5, did not differ from the control plants. The results show that one cannot predict the phenotypic effect of a cellulose synthase gene in a transgenic plant. Given the complex structural/ functional relationship of a functional

cellulose synthase polypeptide, and the limited knowledge in the art regarding how to identify a functional cellulose synthase from a non-functional cellulose synthase, it is unpredictable that each polynucleotide of the genus of the claims (polynucleotides having at least 90% sequence identity to SEQ ID NO: 29, a complementary sequence thereof and antisense sequences of all polynucleotides encoding SEQ ID NO: 30) would have the desired agronomic effect in transgenic plants.

Furthermore, a conservative single amino acid substitution does not result in a predictable result. For example, Lazar et al (Mol. Cell. Biol., Vol. 8, pp. 1247-1252, 1988) showed that the conservative substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while non-conservative substitutions with alanine or asparagine retained the protein function. In the absence of specific guidance as to which nucleotides in SEQ ID NO: 29 would tolerate modifications, one skilled in the art would have to make all possible nucleotide substitutions in the 3444 bp sequence of SEQ ID NO: 29 and test all nucleotide sequences that meet the structural limitations to determine which also meet the functional limitation. One skilled in the art would also have to determine which of these numerous polynucleotides would encode a functional cellulose synthase which can modulate the level of cellulose when expressed in a transgenic plants/plant cells. These tests are considered undue and extensive, as stated in the last Office action.

The instant specification is not enabling for antisense inhibition of the nucleic acids as broadly claimed in claim 2. The specification teaches the antisense of SEQ ID NO: 29. The specification does not teach antisense sequences to all nucleic acids

encoding SEQ ID NO: 30. The state of the art teaches that a high level of sequence identity must exist between the antisense nucleic acid and the target molecule for effective inhibition of expression to occur. Given the degeneracy of the code, many of the nucleic acids that encode SEQ ID NO: 30 share relatively little sequence identity, and are significantly divergent from the nucleic acid of SEQ ID NO: 29. Applicant provides no guidance for inhibition of nucleic acids other than SEQ ID NO: 29 by antisense technology, and Applicant teaches no other target nucleic acids that are endogenous to maize. Applicant has neither amended claim 2 nor argued against this rejection. Examiner also notes that the polynucleotide of claim 1 (d) cannot encode a cellulose synthase because it is a complementary sequence.

Furthermore, the prior art teaches unpredictability in the inhibition of expression of specific coding sequence via antisense RNA in transgenic plants, due to the variation in the degree of antisense inhibition which resulted in different transgenic clones (see, e.g., BIRD et al, Biology and Genetic Review, vol. 9, pages 207-227 (1991)). The antisense expression of tomato polygalacturonase gene taught by Smith et al (Nature, Vol. 334, pp. 724-726 (1988), see, e.g., page 725, paragraph bridging columns 1 and 2) does not produce the predicted change in fruit ripening ( senescence).

*In Genentech Inc v. Novo Nordisk A/S* (42 USPQ2d 1001 at p. 1005). The CAFC stated, "(P)atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable....While every aspect of generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be

provided in order to enable members of the public to understand and carry out the invention....[w]hen there is no disclosure of any specific starting material or conditions under which a process can be carried out, undue experimentation is required...." In this case Applicant is expecting others to identify conservative residues of cellulose synthase that would tolerate modifications in order to generate polynucleotides having the structural properties as recited in the claims (90% identity to SEQ ID NO: 29). Applicant is also expecting others to determine if the polynucleotides encode functional cellulose synthase when expressed in a transgenic plant. Under the guidelines set forth in *Genentech*, this constitutes under experimentation.

See also *in re Fischer, 166 USPQ 19 24 (CCPA 1970)* where the court required that the scope of the claims must bear a reasonable correlation with the scope of the enablement. In this case, the enablement is limited to SEQ ID NO: 29 and the antisense of SEQ ID NO: 29.

Therefore, for all the reasons stated above and in the last Office action, the claimed invention is not enabled throughout the broad scope. Therefore, rejection is maintained.

***Remarks***

The claims are deemed free of the prior art of record.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Medina A. Ibrahim whose telephone number is (571) 272-0797. The Examiner can normally be reached Monday -Thursday from 8:00AM to 5:30PM and every other Friday from 9:00AM to 5:00 PM. Before and after final responses should be directed to fax nos. (703) 872-9306 and (703) 872-9307, respectively.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Amy Nelson, can be reached at (571) 272-0804.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

8/17/05

Mai

MEDINA A. IBRAHIM
PATENT EXAMINER